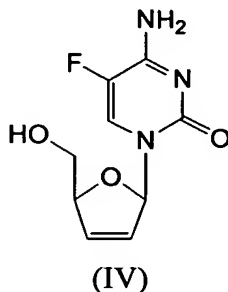


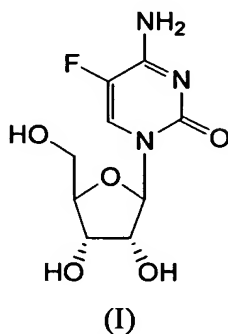
WE CLAIM:

1. A process for the preparation of a compound of Formula (IV):



comprising:

- (1) contacting a compound of Formula (I):



with an acyl halide of Formula  $Q-C(=O)X$ , wherein:

Q is 2-( $R^1CH_2CO_2$ )phenyl-,  $R^1CH_2$ -, or  $R^1CH_2C(=O)OC(R^2)_2$ ;

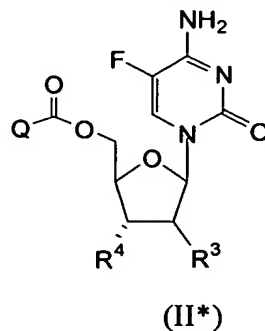
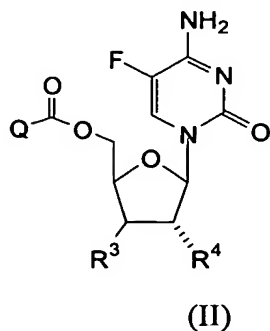
X is Cl, Br, or I;

$R^1$  is H or  $C_1$ - $C_6$  alkyl;

$R^2$ , at each occurrence, is independently selected from methyl, ethyl, and propyl;

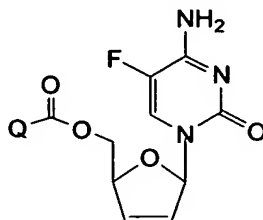
in a suitable polar aprotic solvent to form a compound of Formula (II), a

compound of Formula (II\*), or a mixture of compounds of Formula (II) and (II\*):



wherein  $R^3$  is X; and  $R^4$  is  $R^1CH_2C(=O)O$ -;

(2) contacting the compound of Formula (II), the compound of Formula (II\*), or the mixture of compounds of Formula (II) and (II\*); with a suitable reducing agent in a suitable polar solvent, optionally in the presence of a suitable acid catalyst, to form a compound of Formula (III):



(III); and

(3) contacting the compound of Formula (III) with a suitable base to form the compound of Formula (IV).

2. The process of Claim 1 for the preparation of a compound of Formula (IV), wherein:

in step (1) the acyl halide of Formula Q-C(=O)X comprises:

2-acetoxy-2-methyl-propionyl bromide, 2-(acetoxy)-2-methyl-butanoyl bromide, 2-(acetoxy)-2-ethyl-butanoyl bromide, or 2-(acetoxy)-2-methyl-pentanoyl bromide;

in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent or a combination of two or more polar aprotic solvents; and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl methyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;

in step (2), the suitable reducing agent is selected from the group consisting of: Fe, Zn-Cu couple and Zn;

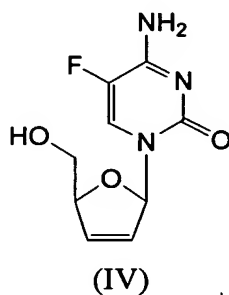
in step (2), the suitable acid catalyst, when present, is selected from the group consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic acid, HCl, HBr, HI, and H<sub>2</sub>SO<sub>4</sub>;

in step (2), the suitable polar solvent comprises one polar solvent or a combination of two or more polar solvents; and is selected from the group consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate,

butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy ethane, and 2-methoxyethyl ether; and

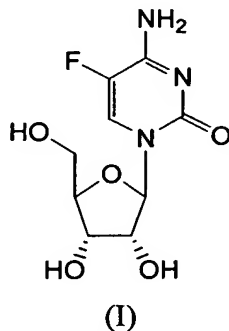
in step (3) the suitable base is selected from the group consisting of: sodium hydroxide, lithium hydroxide, potassium carbonate, sodium carbonate, sodium methoxide, sodium ethoxide, C<sub>3</sub>-C<sub>6</sub> alkyl primary amine, ammonium hydroxide, and ammonium C<sub>1</sub>-C<sub>6</sub> alkoxide.

3. The process according to Claim 1, for the preparation of a compound of Formula (IV):

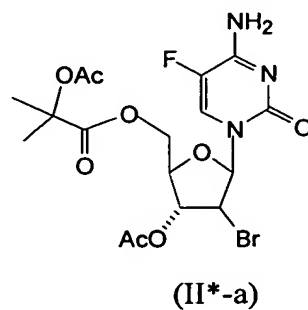
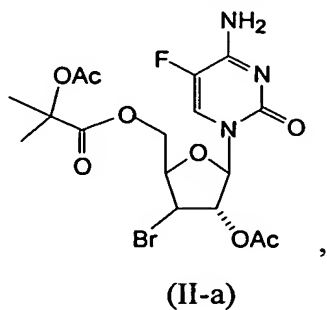


comprising:

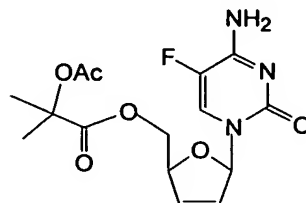
- (1) contacting a compound of Formula (I):



with 2-acetoxy-2-methyl-propionyl bromide in a suitable polar aprotic solvent to form a compound of Formula (II-a), a compound of Formula (II\*-a), or a mixture of compounds of Formula (II-a) and (II\*-a):



(2) contacting the compound of Formula (II-a), the compound of Formula (II\*-a), or the mixture of compounds of Formula (II-a) and (II\*-a); with a suitable reducing agent in a suitable polar solvent, optionally in the presence of a suitable acid catalyst, to form a compound of Formula (III-a):



(III-a); and

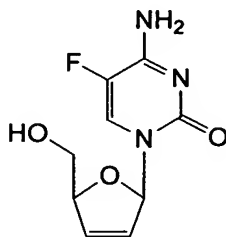
(3) contacting the compound of Formula (III-a) with a suitable base to form the compound of Formula (IV).

4. The process of Claim 3 for the preparation of a compound of Formula (IV), wherein:
- in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent or a combination of two or more polar aprotic solvents; and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl methyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;
  - in step (2), the suitable reducing agent is selected from the group consisting of: Fe, Zn-Cu couple and Zn;
  - in step (2), the suitable acid catalyst, when present, is selected from the group consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic acid, HCl, HBr, HI, and H<sub>2</sub>SO<sub>4</sub>;
  - in step (2), the suitable polar solvent comprises one polar solvent or a combination of two or more polar solvents; and is selected from the group consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate, butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy ethane, and 2-methoxyethyl ether; and
  - in step (3) the suitable base is selected from the group consisting of: sodium hydroxide, lithium hydroxide, potassium carbonate, sodium carbonate,

sodium methoxide, sodium ethoxide, C<sub>3</sub>-C<sub>6</sub> alkyl primary amine, ammonium hydroxide, and ammonium C<sub>1</sub>-C<sub>6</sub> alkoxide.

5. The process of Claim 4 for the preparation of a compound of Formula (IV), wherein:
- in step (1), the suitable polar aprotic solvent comprises a combination of acetonitrile and ethyl acetate;
  - in step (2), the suitable reducing agent is Zn-Cu couple;
  - in step (2), the suitable acid catalyst, when present, is acetic acid;
  - in step (2), the suitable polar solvent comprises a combination of methanol and ethyl acetate; and
  - in step (3) the suitable base is sodium methoxide.

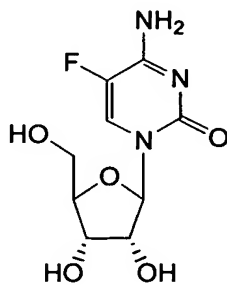
6. The process according to Claim 5, for the preparation of a compound of Formula (IV):



(IV)

comprising:

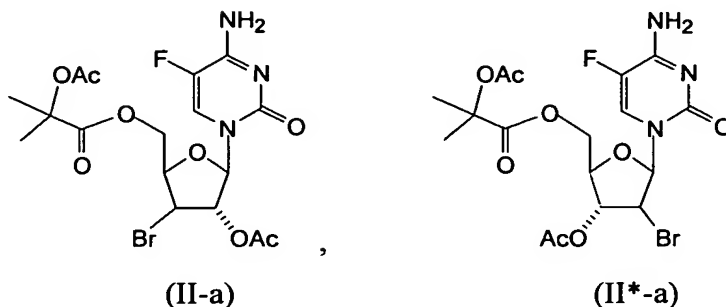
- (1) contacting a compound of Formula (I):



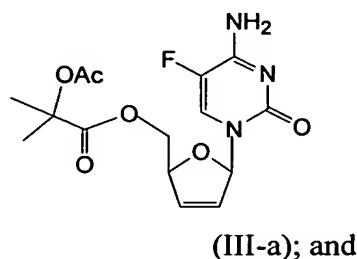
(I)

with 2-acetoxy-2-methyl-propionyl bromide in a suitable polar aprotic solvent comprising a combination of acetonitrile and ethyl acetate, wherein the ratio of acetonitrile to ethyl acetate is 1:4; to form a compound of Formula (II-a), a

compound of Formula (II\*-a), or a mixture of compounds of Formula (II-a) and (II\*-a):

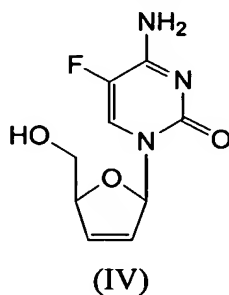


(2) contacting the compound of Formula (II-a), the compound of Formula (II\*-a), or the mixture of compounds of Formula (II-a) and (II\*-a); with Zn-Cu couple in a suitable polar solvent comprising a combination of methanol and ethyl acetate, wherein the ratio of methanol to ethyl acetate is in the range of 1:2 to 1:4; optionally in the presence of acetic acid, to form a compound of Formula (III-a):



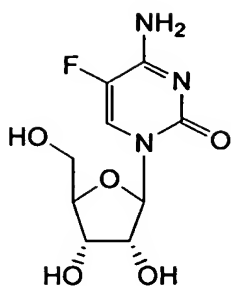
(3) contacting the compound of Formula (III-a) with sodium methoxide to form the compound of Formula (IV).

7. The process of Claim 1 for the preparation of a compound of Formula (IV):



comprising:

(1) contacting a compound of Formula (I):



(I)

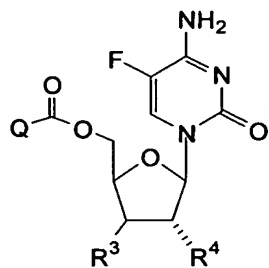
with an acyl halide of Formula  $Q-C(=O)X$ , wherein:

$Q$  is  $R^1CH_2C(=O)OC(R^2)_2$ ;

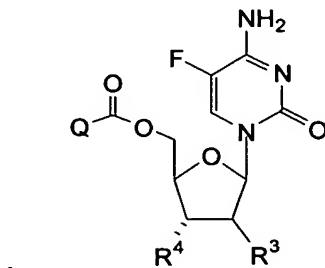
$X$  is Cl, Br, or I;

$R^1$  is H,  $CH_3$ ,  $CH_2CH_3$ , or  $CH_2CH_2CH_3$ ;

$R^2$ , at each occurrence, is independently selected from methyl, ethyl, and propyl; in a suitable polar aprotic solvent to form a compound of Formula (II) or a compound of Formula (II\*):



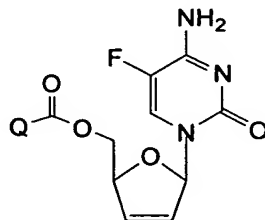
(II)



(II\*)

wherein  $R^3$  is X; and  $R^4$  is  $R^1CH_2C(=O)O$ ;

(2) contacting the compound of Formula (II) or the compound of Formula (II\*) with a suitable reducing agent in a suitable polar solvent, optionally in the presence of a suitable acid catalyst, to form a compound of Formula (III):



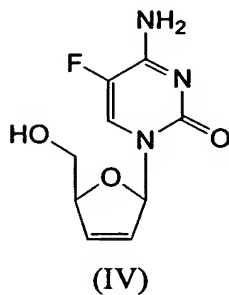
(III); and

(3) contacting the compound of Formula (III) with a suitable base to form the compound of Formula (IV).

8. The process of Claim 7 for the preparation of a compound of Formula (IV), wherein:
- in step (1) the acyl halide of Formula  $Q-C(=O)X$  comprises:
- 2-acetoxy-2-methyl-propionyl bromide, 2-(acetoxy)-2-methyl-butanoyl bromide, 2-(acetoxy)-2-ethyl-butanoyl bromide, or 2-(acetoxy)-2-methyl-pentanoyl bromide;
- in step (1), the suitable polar aprotic solvent comprises
- one polar aprotic solvent or a combination of two or more polar aprotic solvents; and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl methyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;
- in step (2), the suitable reducing agent is selected from the group consisting of:
- Fe, Zn-Cu couple and Zn;
- in step (2), the suitable acid catalyst, when present, is selected from the group consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic acid, HCl, HBr, HI, and  $H_2SO_4$ ;
- in step (2), the suitable polar solvent comprises
- one polar solvent or a combination of two or more polar solvents; and is selected from the group consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate, butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy ethane, and 2-methoxyethyl ether; and
- in step (3) the suitable base is selected from the group consisting of: sodium hydroxide, lithium hydroxide, potassium carbonate, sodium carbonate, sodium methoxide, sodium ethoxide,  $C_3-C_6$  alkyl primary amine, ammonium hydroxide, and ammonium  $C_1-C_6$  alkoxide.

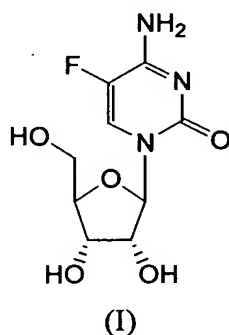


9. The process according to Claim 7, for the preparation of a compound of Formula (IV):

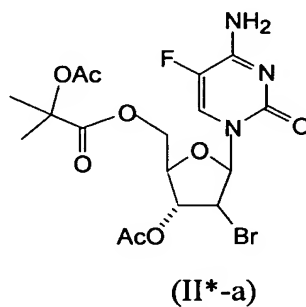
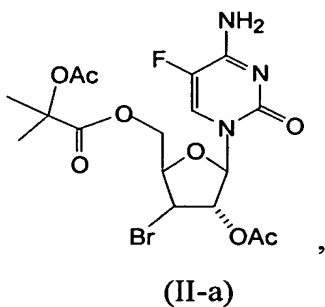


comprising:

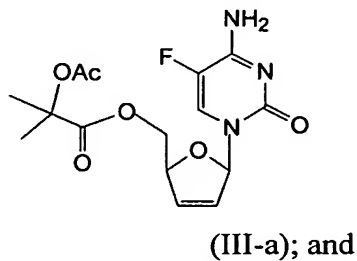
- (1) contacting a compound of Formula (I):



with 2-acetoxy-2-methyl-propionyl bromide in a suitable polar aprotic solvent to form a compound of Formula (II-a) or a compound of Formula (II\*-a):



- (2) contacting the compound of Formula (II-a) or the compound of Formula (II\*-a) with a suitable reducing agent in a suitable polar solvent, optionally in the presence of a suitable acid catalyst, to form a compound of Formula (III-a):



(3) contacting the compound of Formula (III-a) with a suitable base to form the compound of Formula (IV).

10. The process of Claim 9 for the preparation of a compound of Formula (IV), wherein:

in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent or a combination of two or more polar aprotic solvents; and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl methyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;

in step (2), the suitable reducing agent is selected from the group consisting of: Fe, Zn-Cu couple and Zn;

in step (2), the suitable acid catalyst, when present, is selected from the group consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic acid, HCl, HBr, HI, and H<sub>2</sub>SO<sub>4</sub>;

in step (2), the suitable polar solvent comprises one polar solvent or a combination of two or more polar solvents; and is selected from the group consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate, butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy ethane, and 2-methoxyethyl ether; and

in step (3) the suitable base is selected from the group consisting of: sodium hydroxide, lithium hydroxide, potassium carbonate, sodium carbonate, sodium methoxide, sodium ethoxide, C<sub>3</sub>-C<sub>6</sub> alkyl primary amine, ammonium hydroxide, and ammonium C<sub>1</sub>-C<sub>6</sub> alkoxide.

11. The process of Claim 10 for the preparation of a compound of Formula (IV), wherein:

in step (1), the suitable polar aprotic solvent comprises a combination of acetonitrile and ethyl acetate;

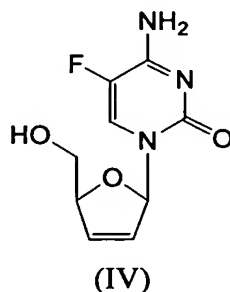
in step (2), the suitable reducing agent is Zn-Cu couple;

in step (2), the suitable acid catalyst, when present, is acetic acid;

in step (2), the suitable polar solvent comprises a combination of methanol and ethyl acetate; and

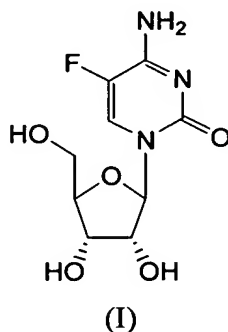
in step (3) the suitable base is sodium methoxide.

12. The process according to Claim 11, for the preparation of a compound of Formula (IV):

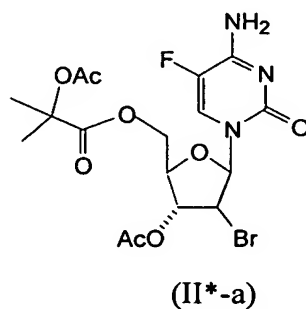
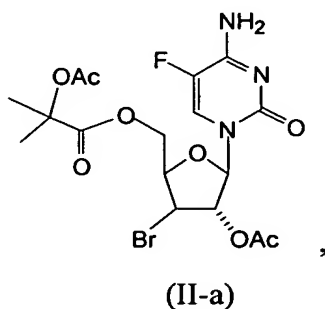


comprising:

- (1) contacting a compound of Formula (I):

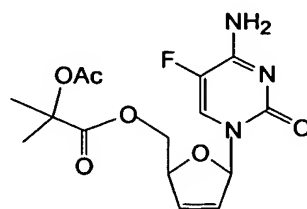


with 2-acetoxy-2-methyl-propionyl bromide in a suitable polar aprotic solvent comprising a combination of acetonitrile and ethyl acetate, wherein the ratio of acetonitrile to ethyl acetate is 1:4; to form a compound of Formula (II-a) or a compound of Formula (II\*-a):



- (2) contacting the compound of Formula (II-a) or the compound of Formula (II\*-a); with Zn-Cu couple in a suitable polar solvent comprising a combination of

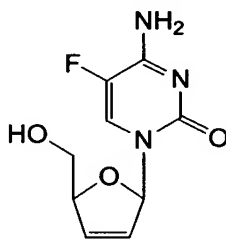
methanol and ethyl acetate, wherein the ratio of methanol to ethyl acetate is in the range of 1:2 to 1:4; optionally in the presence of acetic acid, to form a compound of Formula (III-a):



(III-a); and

(3) contacting the compound of Formula (III-a) with sodium methoxide to form the compound of Formula (IV).

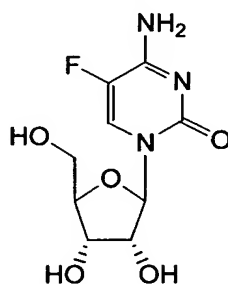
13. The process of Claim 1 for the preparation of a compound of Formula (IV):



(IV)

comprising:

(1) contacting a compound of Formula (I):



(I)

with an acyl halide of Formula  $Q-C(=O)X$ , wherein:

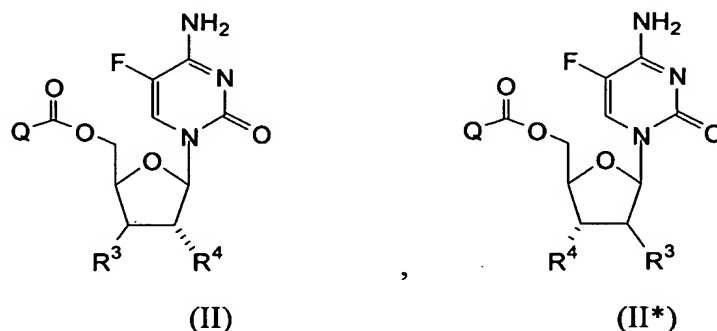
$Q$  is  $R^1CH_2C(=O)OC(R^2)_2$ ;

$X$  is  $Cl$ ,  $Br$ , or  $I$ ;

$R^1$  is  $H$ ,  $CH_3$ ,  $CH_2CH_3$ , or  $CH_2CH_2CH_3$ ;

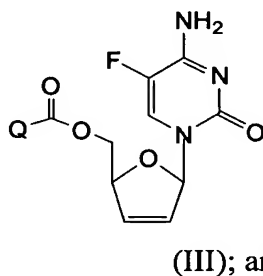
$R^2$ , at each occurrence, is independently selected from methyl, ethyl, and propyl;

in a suitable polar aprotic solvent to form a mixture of compounds of Formula (II) and (II\*):



wherein  $R^3$  is X; and  $R^4$  is  $R^1CH_2C(=O)O-$ ;

(2) contacting the mixture of compounds of Formula (II) and (II\*) with a suitable reducing agent in a suitable polar solvent, optionally in the presence of a suitable acid catalyst, to form a compound of Formula (III):



(3) contacting the compound of Formula (III) with a suitable base to form the compound of Formula (IV).

14. The process of Claim 13 for the preparation of a compound of Formula (IV), wherein:

in step (1) the acyl halide of Formula  $Q-C(=O)X$  comprises:

2-acetoxy-2-methyl-propionyl bromide, 2-(acetoxy)-2-methyl-butanoyl bromide, 2-(acetoxy)-2-ethyl-butanoyl bromide, or 2-(acetoxy)-2-methyl-pentanoyl bromide;

in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent or a combination of two or more polar aprotic solvents; and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl methyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;

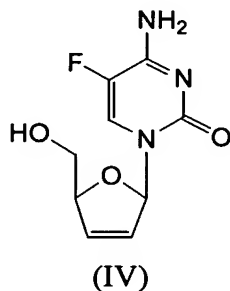
in step (2), the suitable reducing agent is selected from the group consisting of:  
Fe, Zn-Cu couple and Zn;

in step (2), the suitable acid catalyst, when present, is selected from the group  
consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid,  
toluene sulfonic acid, HCl, HBr, HI, and H<sub>2</sub>SO<sub>4</sub>;

in step (2), the suitable polar solvent comprises one polar solvent or a  
combination of two or more polar solvents; and is selected from the group  
consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate,  
butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy  
ethane, and 2-methoxyethyl ether; and

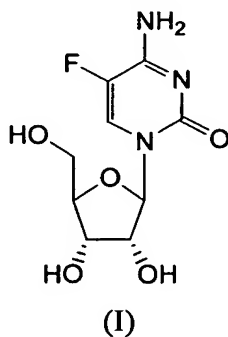
in step (3) the suitable base is selected from the group consisting of: sodium  
hydroxide, lithium hydroxide, potassium carbonate, sodium carbonate,  
sodium methoxide, sodium ethoxide, C<sub>3</sub>-C<sub>6</sub> alkyl primary amine,  
ammonium hydroxide, and ammonium C<sub>1</sub>-C<sub>6</sub> alkoxide.

15. The process according to Claim 19, for the preparation of a compound of  
Formula (IV):

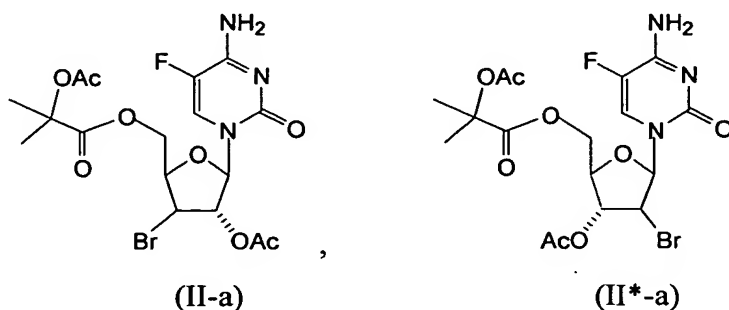


comprising:

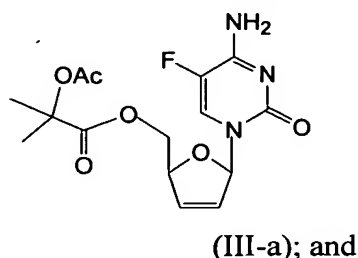
- (1) contacting a compound of Formula (I):



with 2-acetoxy-2-methyl-propionyl bromide in a suitable polar aprotic solvent to form a mixture of compounds of Formula (II-a) and (II\*-a):



(2) contacting the mixture of compounds of Formula (II-a) and (II\*-a) with a suitable reducing agent in a suitable polar solvent, optionally in the presence of a suitable acid catalyst, to form a compound of Formula (III-a):



(3) contacting the compound of Formula (III-a) with a suitable base to form the compound of Formula (IV).

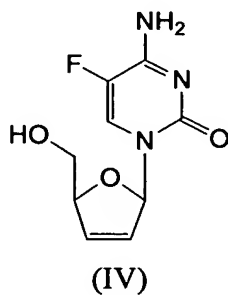
16. The process of Claim 15 for the preparation of a compound of Formula (IV), wherein:
- in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent or a combination of two or more polar aprotic solvents; and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl methyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;
  - in step (2), the suitable reducing agent is selected from the group consisting of: Fe, Zn-Cu couple and Zn;
  - in step (2), the suitable acid catalyst, when present, is selected from the group consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic acid, HCl, HBr, HI, and H<sub>2</sub>SO<sub>4</sub>;

in step (2), the suitable polar solvent comprises one polar solvent or a combination of two or more polar solvents; and is selected from the group consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate, butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy ethane, and 2-methoxyethyl ether; and

in step (3) the suitable base is selected from the group consisting of: sodium hydroxide, lithium hydroxide, potassium carbonate, sodium carbonate, sodium methoxide, sodium ethoxide, C<sub>3</sub>-C<sub>6</sub> alkyl primary amine, ammonium hydroxide, and ammonium C<sub>1</sub>-C<sub>6</sub> alkoxide.

17. The process of Claim 16 for the preparation of a compound of Formula (IV), wherein:
- in step (1), the suitable polar aprotic solvent comprises a combination of acetonitrile and ethyl acetate;
- in step (2), the suitable reducing agent is Zn-Cu couple;
- in step (2), the suitable acid catalyst, when present, is acetic acid;
- in step (2), the suitable polar solvent comprises a combination of methanol and ethyl acetate; and
- in step (3) the suitable base is sodium methoxide.

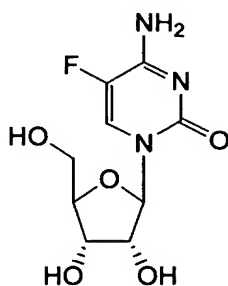
18. The process according to Claim 17, for the preparation of a compound of Formula (IV):



comprising:

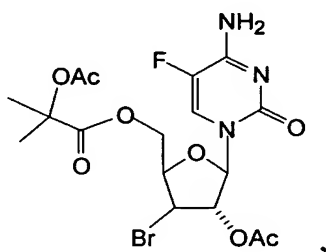


(1) contacting a compound of Formula (I):

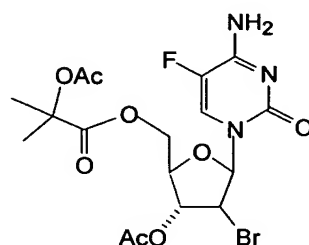


(I)

with 2-acetoxy-2-methyl-propionyl bromide in a suitable polar aprotic solvent comprising a combination of acetonitrile and ethyl acetate, wherein the ratio of acetonitrile to ethyl acetate is 1:4; to form a mixture of compounds of Formula (II-a) and (II\*-a):

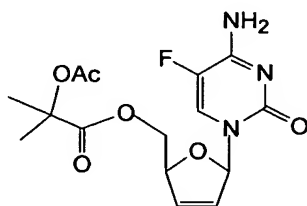


(II-a)



(II\*-a)

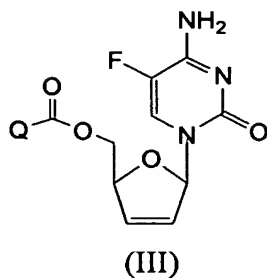
(2) contacting the mixture of compounds of Formula (II-a) and (II\*-a) with Zn-Cu couple in a suitable polar solvent comprising a combination of methanol and ethyl acetate, wherein the ratio of methanol to ethyl acetate is in the range of 1:2 to 1:4; optionally in the presence of acetic acid, to form a compound of Formula (III-a):



(III-a); and

(3) contacting the compound of Formula (III-a) with sodium methoxide to form the compound of Formula (IV).

19. A process for the preparation of a compound of Formula (III):



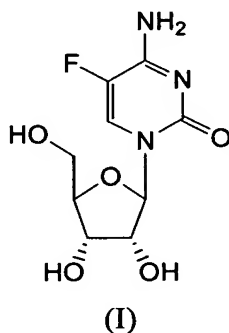
wherein:

Q is 2-(R<sup>1</sup>CH<sub>2</sub>CO<sub>2</sub>)phenyl-, R<sup>1</sup>CH<sub>2</sub>-, or R<sup>1</sup>CH<sub>2</sub>C(=O)OC(R<sup>2</sup>)<sub>2</sub>-;

R<sup>1</sup> is H or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sup>2</sup>, at each occurrence, is independently selected from methyl, ethyl, and propyl;  
comprising:

(1) contacting a compound of Formula (I):



with an acyl halide of Formula Q-C(=O)X, wherein:

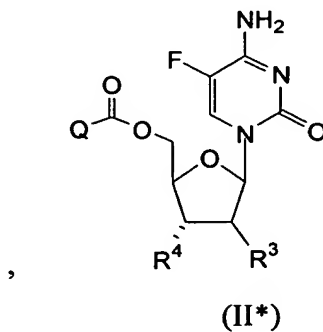
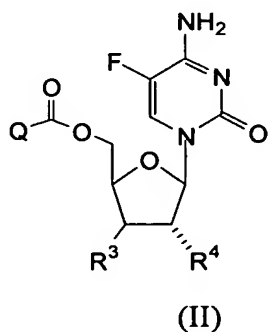
Q is 2-(R<sup>1</sup>CH<sub>2</sub>CO<sub>2</sub>)phenyl-, R<sup>1</sup>CH<sub>2</sub>-, or R<sup>1</sup>CH<sub>2</sub>C(=O)OC(R<sup>2</sup>)<sub>2</sub>-;

X is Cl, Br, or I;

R<sup>1</sup> is H or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sup>2</sup>, at each occurrence, is independently selected from methyl, ethyl, and propyl;

in a suitable polar aprotic solvent to form a compound of Formula (II), a compound of Formula (II\*), or a mixture of compounds of Formula (II) and (II\*):



wherein  $R^3$  is X; and  $R^4$  is  $R^1CH_2C(=O)O-$ ; and

(2) contacting the compound of Formula (II), the compound of Formula (II\*), or the mixture of compounds of Formula (II) and (II\*); with a suitable reducing agent in a suitable polar solvent, optionally in the presence of a suitable acid catalyst, to form a compound of Formula (III).

20. The process of Claim 19 for the preparation of a compound of Formula (III), wherein:

in step (1) the acyl halide of Formula  $Q-C(=O)X$  comprises:

2-acetoxy-2-methyl-propionyl bromide, 2-(acetoxy)-2-methyl-butanoyl bromide, 2-(acetoxy)-2-ethyl-butanoyl bromide, or 2-(acetoxy)-2-methyl-pentanoyl bromide;

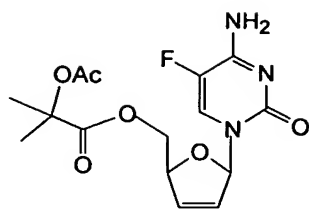
in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent or a combination of two or more polar aprotic solvents; and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl methyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;

in step (2), the suitable reducing agent is selected from the group consisting of: Fe, Zn-Cu couple and Zn;

in step (2), the suitable acid catalyst, when present, is selected from the group consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic acid, HCl, HBr, HI, and  $H_2SO_4$ ; and

in step (2), the suitable polar solvent comprises one polar solvent or a combination of two or more polar solvents; and is selected from the group consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate, butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy ethane, and 2-methoxyethyl ether.

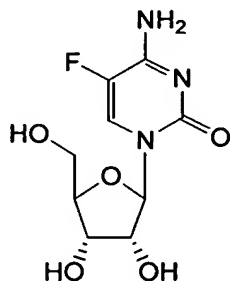
21. The process according to Claim 19, for the preparation of a compound of Formula (III-a):



(III-a)

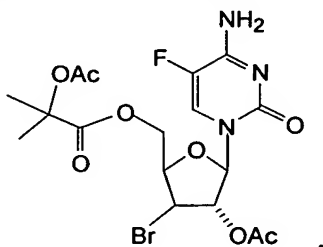
comprising:

(1) contacting a compound of Formula (I):

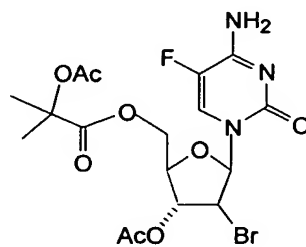


(I)

with 2-acetoxy-2-methyl-propionyl bromide in a suitable polar aprotic solvent to form a compound of Formula (II-a), a compound of Formula (II\*-a), or a mixture of compounds of Formula (II-a) and (II\*-a):



(II-a)



(II\*-a)

(2) contacting the compound of Formula (II-a), the compound of Formula (II\*-a), or the mixture of compounds of Formula (II-a) and (II\*-a); with a suitable reducing agent in a suitable polar solvent, optionally in the presence of a suitable acid catalyst, to form a compound of Formula (III-a).

22. The process of Claim 21 for the preparation of a compound of Formula (III-a), wherein:

in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent or a combination of two or more polar aprotic solvents; and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl

methoxyethyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;

in step (2), the suitable reducing agent is selected from the group consisting of: Fe, Zn-Cu couple and Zn;

in step (2), the suitable acid catalyst, when present, is selected from the group consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic acid, HCl, HBr, HI, and H<sub>2</sub>SO<sub>4</sub>; and

in step (2), the suitable polar solvent comprises one polar solvent or a combination of two or more polar solvents; and is selected from the group consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate, butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy ethane, and 2-methoxyethyl ether.

23. The process of Claim 22 for the preparation of a compound of Formula (III-a), wherein:

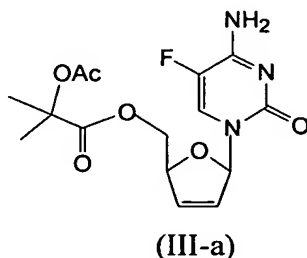
in step (1), the suitable polar aprotic solvent comprises a combination of acetonitrile and ethyl acetate;

in step (2), the suitable reducing agent is Zn-Cu couple;

in step (2), the suitable acid catalyst, when present, is acetic acid; and

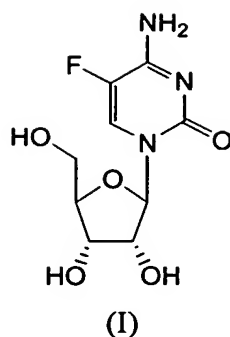
in step (2), the suitable polar solvent comprises a combination of methanol and ethyl acetate.

24. The process according to Claim 23, for the preparation of a compound of Formula (III-a):

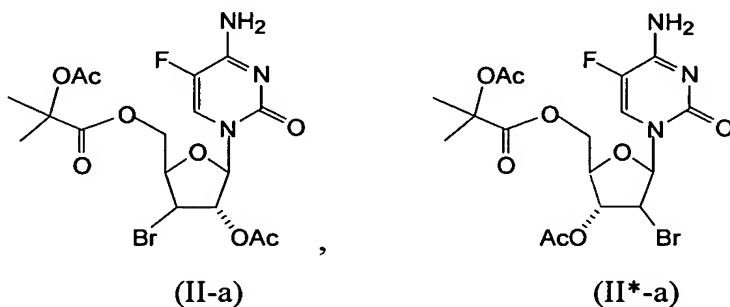


comprising:

(1) contacting a compound of Formula (I):

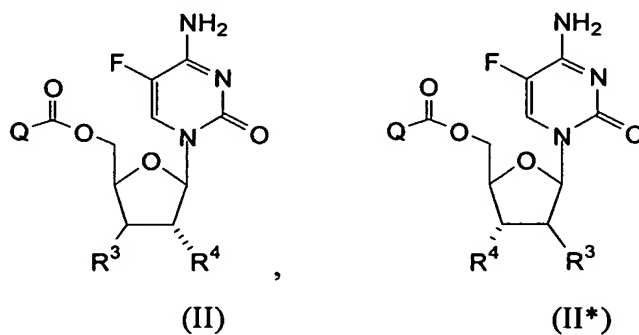


with 2-acetoxy-2-methyl-propionyl bromide in a suitable polar aprotic solvent comprising a combination of acetonitrile and ethyl acetate, wherein the ratio of acetonitrile to ethyl acetate is 1:4; to form a compound of Formula (II-a), a compound of Formula (II\*-a), or a mixture of compounds of Formula (II-a) and (II\*-a):



(2) contacting the compound of Formula (II-a), the compound of Formula (II\*-a), or the mixture of compounds of Formula (II-a) and (II\*-a); with Zn-Cu couple in a suitable polar solvent comprising a combination of methanol and ethyl acetate, wherein the ratio of methanol to ethyl acetate is in the range of 1:2 to 1:4; optionally in the presence of acetic acid, to form a compound of Formula (III-a).

25. A compound of Formula (II) or (II\*):



or a pharmaceutically acceptable salt thereof, wherein:

Q is  $R^1CH_2-$  or  $R^1CH_2C(=O)OC(R^2)_2-$ ;

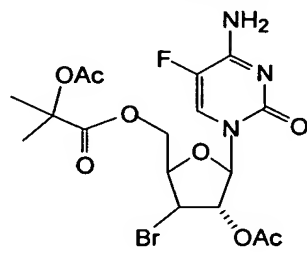
$R^1$  is H or  $C_1-C_6$  alkyl;

$R^2$  is independently selected from methyl, ethyl, and propyl;

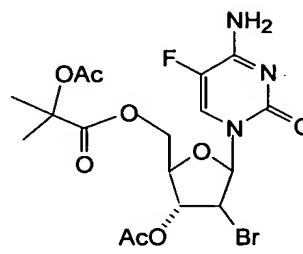
$R^3$  is Cl, Br, or I; and

$R^4$  is  $R^1CH_2C(=O)O-$ .

26. A compound of Claim ~~25~~ of Formula (II-a) or (II\*-a):



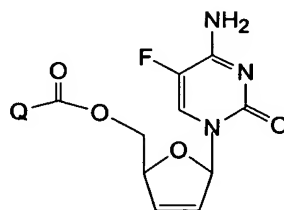
(II-a)



(II\*-a)

or a pharmaceutically acceptable salt thereof.

27. A compound of Formula (III):



(III)

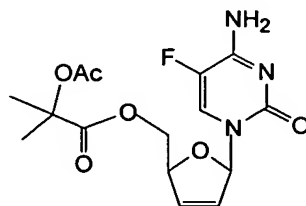
or a pharmaceutically acceptable salt thereof, wherein:

Q is  $R^1CH_2-$  or  $R^1CH_2C(=O)OC(R^2)_2-$ ;

$R^1$  is H or  $C_1-C_6$  alkyl; and

$R^2$  is independently selected from methyl, ethyl, and propyl.

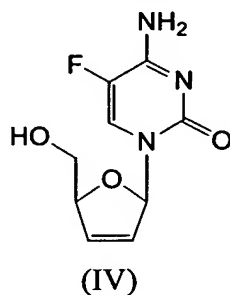
28. A compound of Claim ~~27~~ of Formula (III-a):



(III-a)

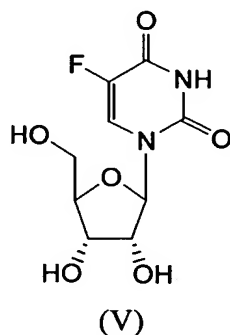
or a pharmaceutically acceptable salt thereof.

29. A process for the preparation of a compound of Formula (IV):



comprising:

- (1) contacting a compound of Formula (IV):



with an acyl halide of Formula  $Q-C(=O)X$ , wherein:

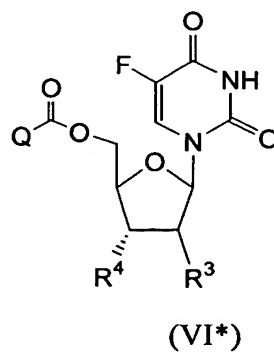
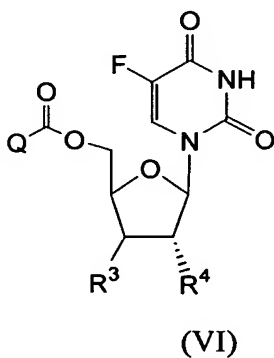
Q is 2-( $R^1CH_2CO_2$ )phenyl-,  $R^1CH_2$ -, or  $R^1CH_2C(=O)OC(R^2)_2$ ;

X is Cl, Br, or IV;

$R^1$  is H or  $C_1$ - $C_6$  alkyl;

$R^2$ , at each occurrence, is independently selected from methyl, ethyl, and propyl;

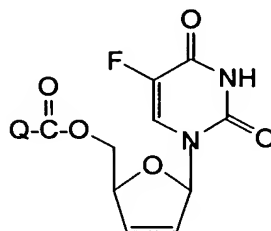
in a suitable polar aprotic solvent to form a compound of Formula (VI), a compound of Formula (VI\*), or a mixture of compounds of Formula (VI) and (VI\*):





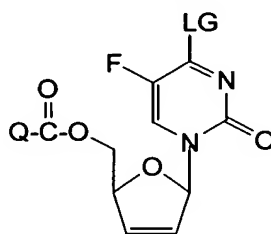
wherein  $R^3$  is X; and  $R^4$  is  $R^1CH_2C(=O)O-$ ;

(2) contacting the compound of Formula (VI), the compound of Formula (VI\*), or the mixture of compounds of Formula (VI) and (VI\*); with a reducing agent in a suitable polar solvent, optionally in the presence of an acid catalyst, to form a compound of Formula (VII):



(VII);

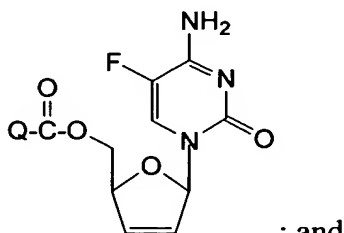
(3a) contacting the compound of Formula (VII) with an activating agent in the presence of an amine base, to form a compound of Formula (VIII):



(VIII)

wherein LG is a leaving group derived from the activating agent;

(3b) contacting the compound of Formula (VIII) with an aminating agent to form a compound of Formula (III),



; and

(III)

(4) contacting the compound of Formula (III) with a suitable base to form the compound of Formula (IV).

30. The process of Claim 29 for the preparation of a compound of Formula (IV), wherein:

in step (1) the acyl halide of Formula  $Q-C(=O)X$  comprises:

2-acetoxy-2-methyl-propionyl bromide,  
2-(acetoxy)-2-methyl-butanoyl bromide,  
2-(acetoxy)-2-ethyl-butanoyl bromide, or  
2-(acetoxy)-2-methyl-pentanoyl bromide;

in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent or a combination of two or more polar aprotic solvents, and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl methyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;

in step (2), the reducing agent is selected from the group consisting of: Fe, Zn-Cu couple and Zn;

in step (2), the acid catalyst, when present, is selected from the group consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic acid, HCl, HBr, HI, and  $H_2SO_4$ ;

in step (2), the suitable polar solvent comprises one polar solvent or a combination of two or more polar solvents; and is selected from the group consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate, butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy ethane, and 2-methoxyethyl ether;

in step (3a) the activating agent is selected from the group consisting of: methanesulfonyl chloride, trifluoromethyl sulfonyl chloride, ethanesulfonyl chloride, benzenesulfonyl chloride, p-toluene-sulfonyl chloride, triazole/phosphorus oxychloride and triazole/diphenyl chloro-phosphate;

in step (3a) the amine base is selected from the group consisting of: triethylamine, tributylamine, N-methylmorpholine, N,N-diisopropyl-ethylamine, N,N-dimethylcyclohexylamine, N,N-diethylcyclohexylamine, N,N-dimethyloctylamine, tetramethylethylenediamine, pyridine, N,N-dimethyl-aminopyridine,

1,4-diazabicyclo[2.2.2]octane,  
1,8-diazabicyclo[5.4.0]undec-7-ene, and  
1,5-diazabicyclo[4.3.0]non-5-ene;

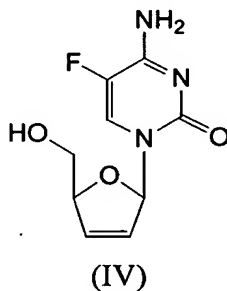
in step (3a) the leaving group LG is selected from the group consisting of  
methanesulfonyloxy, trifluoromethyl-sulfonyloxy, ethanesulfonyloxy,  
benzenesulfonyloxy, toluenesulfonyloxy, and triazolyl;

in step (3b) the aminating agent is selected

from the group consisting of:  $\text{NH}_3$ , ammonium hydroxide, and ammonium  
carbonate; and

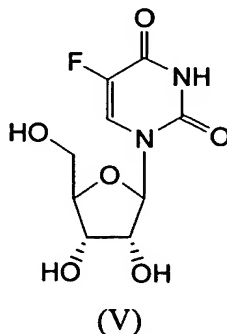
in step (4) the suitable base is selected from the group consisting of: sodium  
hydroxide, lithium hydroxide, potassium carbonate, sodium carbonate,  
sodium methoxide, sodium ethoxide,  $\text{C}_3\text{-C}_6$  alkyl primary amine,  
ammonium hydroxide, and ammonium  $\text{C}_1\text{-C}_6$  alkoxide.

31. The process according to Claim 29, for the preparation of a compound of  
Formula (IV):

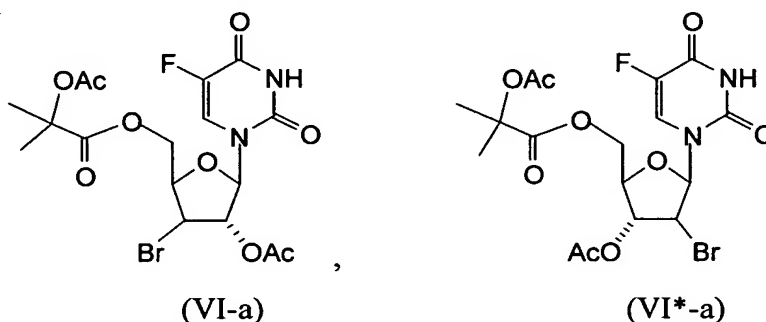


comprising:

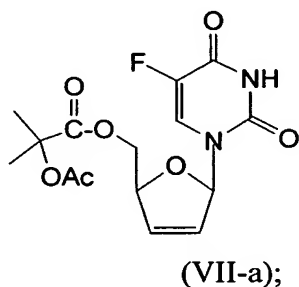
- (1) contacting a compound of Formula (V):



with 2-acetoxy-2-methyl-propionyl bromide in a suitable polar aprotic solvent to form a compound of Formula (VI-a), a compound of Formula (VI\*-a), or a mixture of compounds of Formula (VI-a) and (VI\*-a):



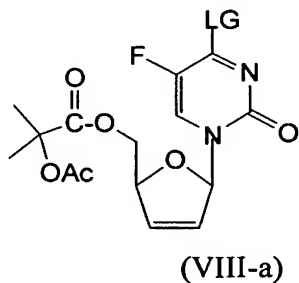
(2) contacting the compound of Formula (VI-a), the compound of Formula (VI\*-a), or the mixture of compounds of Formula (VI-a) and (VI\*-a); with a reducing agent in a suitable polar solvent, optionally in the presence of an acid catalyst, to form a compound of Formula (VII-a):



(3a) contacting the compound of Formula (VII-a) with an activating agent selected from the group consisting of:

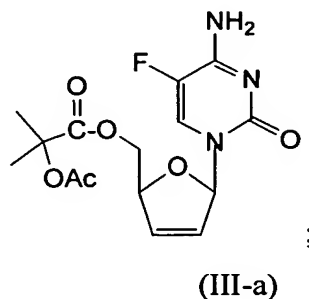
- i) an aryl sulfonyl halide,
- ii) an alkyl sulfonyl halide, and
- iii) 1,2,4-triazole in the presence of a phosphorus chloride;

in the presence of an amine base, to form a compound of Formula (VIII-a);



wherein LG is a leaving group derived from the activating agent;

(3b) contacting the compound of Formula (VIII-a) with an aminating agent to form a compound of Formula (III-a),



and

(4) contacting the compound of Formula (III-a) with a suitable base to form the compound of Formula (IV).

32. The process of Claim 31 for the preparation of a compound of Formula (IV), wherein:

in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent or a combination of two or more polar aprotic solvents; and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl methyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;

in step (2), the reducing agent is selected from the group consisting of: Fe, Zn-Cu couple and Zn;

in step (2), the acid catalyst, when present, is selected from the group consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic acid, HCl, HBr, HI, and H<sub>2</sub>SO<sub>4</sub>;

in step (2), the suitable polar solvent comprises one polar solvent or a combination of two or more polar solvents; and is selected from the group consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate, butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy ethane, and 2-methoxyethyl ether;

in step (3a) the activating agent is selected from the group consisting of: methanesulfonyl chloride, trifluoromethyl sulfonyl chloride, ethanesulfonyl chloride, benzenesulfonyl chloride,

p-toluene-sulfonyl chloride, triazole/phosphorus oxychloride and triazole/diphenyl chloro-phosphate;

in step (3a) the amine base is selected from the group consisting of:

triethylamine, tributylamine,  
 N-methylmorpholine, N,N-diisopropyl-ethylamine,  
 tetramethylethylenediamine, pyridine,  
 N,N-dimethyl-aminopyridine,  
 1,4-diazabicyclo[2.2.2]octane, and  
 1,8-diazabicyclo[5.4.0]undec-7-ene;

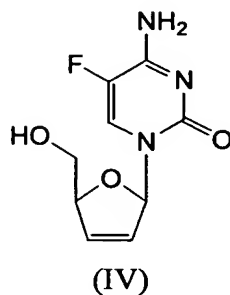
in step (3a) the leaving group LG is selected from the group consisting of  
 methanesulfonyloxy, trifluoromethyl-sulfonyloxy, ethanesulfonyloxy,  
 benzenesulfonyloxy, toluenesulfonyloxy, and triazolyl;

in step (3b) the aminating agent is selected  
 from the group:  $\text{NH}_3$ , ammonium hydroxide, and ammonium carbonate;  
 and

in step (4) the suitable base is selected from the group consisting of: sodium hydroxide, lithium hydroxide, potassium carbonate, sodium carbonate, sodium methoxide, sodium ethoxide,  $\text{C}_3\text{-C}_6$  alkyl primary amine, ammonium hydroxide, and ammonium  $\text{C}_1\text{-C}_6$  alkoxide.

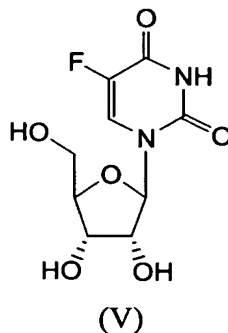
33. The process of Claim 32 for the preparation of a compound of Formula (IV), wherein:
- in step (1), the suitable polar aprotic solvent comprises one solvent which is acetonitrile;
- in step (2), the reducing agent is Zn-Cu couple;
- in step (2), the acid catalyst, when present, is acetic acid;
- in step (2), the suitable polar solvent comprises a combination of methanol and ethyl acetate;
- in step (3a) the activating agent is triazole/phosphorus oxychloride;
- in step (3a) the amine base is triethylamine;
- in step (3a) the leaving group LG is triazolyl;
- in step (3b), the aminating agent is  $\text{NH}_3$ ; and
- in step (4) the suitable base is sodium methoxide.

34. The process according to Claim 33, for the preparation of a compound of Formula (IV):

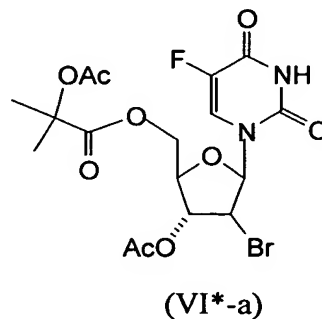
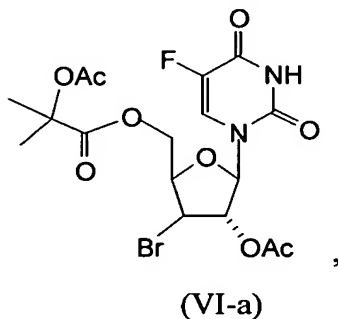


comprising:

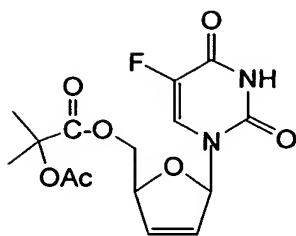
- (1) contacting a compound of Formula (V):



with 2-acetoxy-2-methyl-propionyl bromide in acetonitrile to form a compound of Formula (VI-a), a compound of Formula (VI\*-a), or a mixture of compounds of Formula (VI-a) and (VI\*-a):

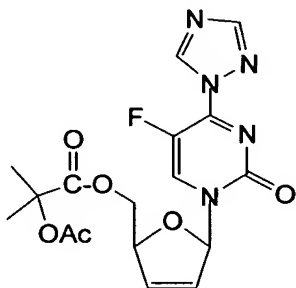


- (2) contacting the compound of Formula (VI-a), the compound of Formula (VI\*-a), or the mixture of compounds of Formula (VI-a) and (VI\*-a); with Zn-Cu couple in a suitable polar solvent comprising a combination of methanol and ethyl acetate, wherein the ratio of methanol to ethyl acetate is in the range of 1:2 to 1:4; optionally in the presence of acetic acid, to form a compound of Formula (VII-a):



(VII-a);

(3a) contacting the compound of Formula (VII-a) with 1,2,4-triazole/phosphorus oxychloride, in the presence of triethylamine, to form a compound of Formula (VIII-a):

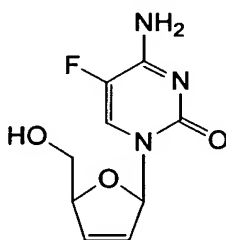


(VIII-a);

(3b) contacting the compound of Formula (VIII-a) with  $\text{NH}_3$ , to form a compound of Formula (III-a), and

(4) contacting the compound of Formula (III-a) with sodium methoxide to form the compound of Formula (IV).

35. The process of Claim 29 for the preparation of a compound of Formula (IV):

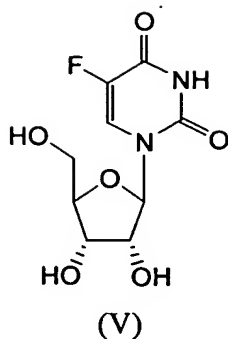


(IV)

comprising:

(1) contacting a compound of Formula (V):





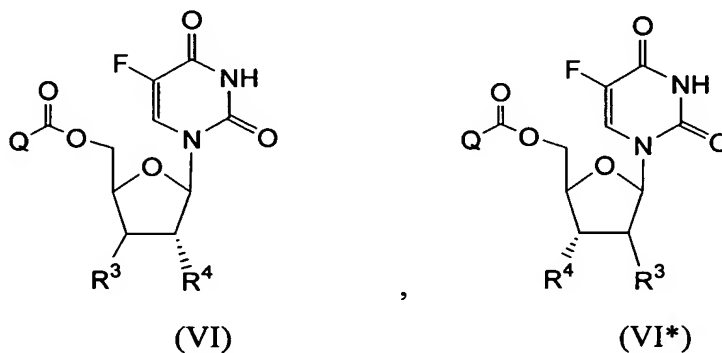
with an acyl halide of Formula  $Q-C(=O)X$ , wherein:

$Q$  is 2-( $R^1CH_2CO_2$ )phenyl-,  $R^1CH_2-$ , or  $R^1CH_2C(=O)OC(R^2)_2-$ ;

$X$  is Cl, Br, or IV;

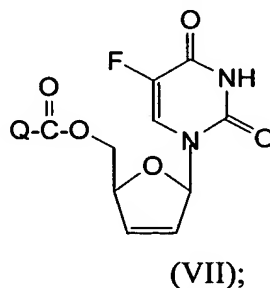
$R^1$  is H or  $C_1-C_6$  alkyl;

$R^2$ , at each occurrence, is independently selected from methyl, ethyl, and propyl;  
in a suitable polar aprotic solvent to form a mixture of compounds of Formula (VI) and (VI\*):

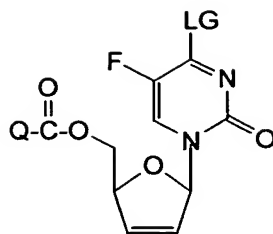


wherein  $R^3$  is X; and  $R^4$  is  $R^1CH_2C(=O)O-$ ;

(2) contacting the mixture of compounds of Formula (VI) and (VI\*); with a reducing agent in a suitable polar solvent, optionally in the presence of an acid catalyst, to form a compound of Formula (VII):



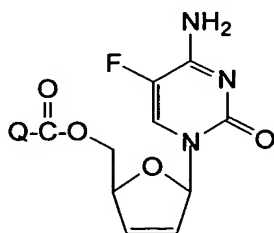
(3a) contacting the compound of Formula (VII) with an activating agent in the presence of an amine base, to form a compound of Formula (VIII):



(VIII)

wherein LG is a leaving group derived from the activating agent;

(3b) contacting the compound of Formula (VIII) with an aminating agent to form a compound of Formula (III),



; and

(III)

(4) contacting the compound of Formula (III) with a suitable base to form the compound of Formula (IV).

36. The process of Claim 35 for the preparation of a compound of Formula (IV), wherein:

in step (1) the acyl halide of Formula  $Q-C(=O)X$  comprises:

- 2-acetoxy-2-methyl-propionyl bromide,
- 2-(acetoxy)-2-methyl-butanoyl bromide,
- 2-(acetoxy)-2-ethyl-butanoyl bromide, or
- 2-(acetoxy)-2-methyl-pentanoyl bromide;

in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent or a combination of two or more polar aprotic solvents, and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl methyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;

in step (2), the reducing agent is selected from the group consisting of: Fe, Zn-Cu couple and Zn;

in step (2), the acid catalyst, when present, is selected from the group consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic acid, HCl, HBr, HI, and H<sub>2</sub>SO<sub>4</sub>;

in step (2), the suitable polar solvent comprises one polar solvent or a combination of two or more polar solvents; and is selected from the group consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate, butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy ethane, and 2-methoxyethyl ether;

in step (3a) the activating agent is selected from the group consisting of: methanesulfonyl chloride, trifluoromethyl sulfonyl chloride, ethanesulfonyl chloride, benzenesulfonyl chloride, p-toluene-sulfonyl chloride, triazole/phosphorus oxychloride and triazole/diphenyl chloro-phosphate;

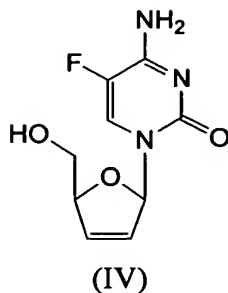
in step (3a) the amine base is selected from the group consisting of: triethylamine, tributylamine, N-methylmorpholine, N,N-diisopropyl-ethylamine, N,N-dimethylcyclohexylamine, N,N-diethylcyclohexylamine, N,N-dimethyloctylamine, tetramethylethylenediamine, pyridine, N,N-dimethyl-aminopyridine, 1,4-diazabicyclo[2.2.2]octane, 1,8-diazabicyclo[5.4.0]undec-7-ene, and 1,5-diazabicyclo[4.3.0]non-5-ene;

in step (3a) the leaving group LG is selected from the group consisting of methanesulfonyloxy, trifluoromethyl-sulfonyloxy, ethanesulfonyloxy, benzenesulfonyloxy, toluenesulfonyloxy, and triazolyl;

in step (3b) the aminating agent is selected from the group consisting of: NH<sub>3</sub>, ammonium hydroxide, and ammonium carbonate; and

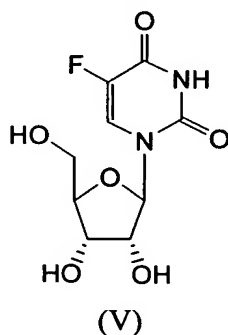
in step (4) the suitable base is selected from the group consisting of: sodium hydroxide, lithium hydroxide, potassium carbonate, sodium carbonate, sodium methoxide, sodium ethoxide, C<sub>3</sub>-C<sub>6</sub> alkyl primary amine, ammonium hydroxide, and ammonium C<sub>1</sub>-C<sub>6</sub> alkoxide.

37. The process according to Claim 35, for the preparation of a compound of Formula (IV):

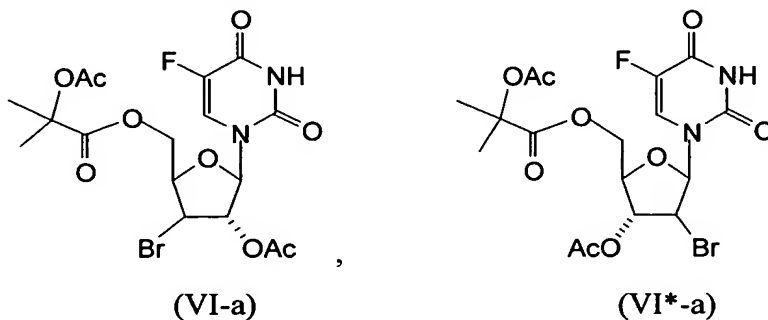


comprising:

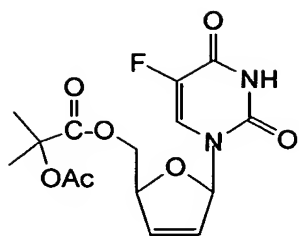
- (1) contacting a compound of Formula (V):



with 2-acetoxy-2-methyl-propionyl bromide in a suitable polar aprotic solvent to form a mixture of compounds of Formula (VI-a) and (VI\*-a):



- (2) contacting the mixture of compounds of Formula (VI-a) and (VI\*-a); with a reducing agent in a suitable polar solvent, optionally in the presence of an acid catalyst, to form a compound of Formula (VII-a):

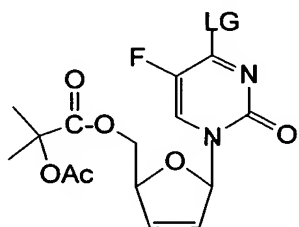


(VII-a);

(3a) contacting the compound of Formula (VII-a) with a activating agent selected from the group consisting of:

- i) an aryl sulfonyl halide,
- ii) an alkyl sulfonyl halide, and
- iii) 1,2,4-triazole in the presence of a phosphorus chloride;

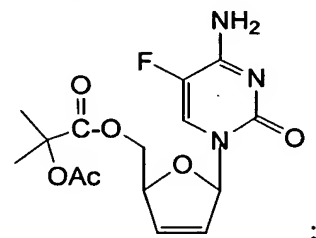
in the presence of an amine base, to form a compound of Formula (VIII-a);



(VIII-a)

wherein LG is a leaving group derived from the activating agent;

(3b) contacting the compound of Formula (VIII-a) with an aminating agent to form a compound of Formula (III-a),



(III-a)

and

(4) contacting the compound of Formula (III-a) with a suitable base to form the compound of Formula (IV).

38. The process of Claim 37 for the preparation of a compound of Formula (IV), wherein:
- in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent or a combination of two or more polar aprotic solvents; and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl methyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;
  - in step (2), the reducing agent is selected from the group consisting of: Fe, Zn-Cu couple and Zn;
  - in step (2), the acid catalyst, when present, is selected from the group consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic acid, HCl, HBr, HI, and H<sub>2</sub>SO<sub>4</sub>;
  - in step (2), the suitable polar solvent comprises one polar solvent or a combination of two or more polar solvents; and is selected from the group consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate, butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy ethane, and 2-methoxyethyl ether;
  - in step (3a) the activating agent is selected from the group consisting of: methanesulfonyl chloride, trifluoromethyl sulfonyl chloride, ethanesulfonyl chloride, benzenesulfonyl chloride, p-toluene-sulfonyl chloride, triazole/phosphorus oxychloride and triazole/diphenyl chloro-phosphate;
  - in step (3a) the amine base is selected from the group consisting of: triethylamine, tributylamine, N-methylmorpholine, N,N-diisopropyl-ethylamine, tetramethylethylenediamine, pyridine, N,N-dimethyl-aminopyridine, 1,4-diazabicyclo[2.2.2]octane, and 1,8-diazabicyclo[5.4.0]undec-7-ene;
  - in step (3a) the leaving group LG is selected from the group consisting of methanesulfonyloxy, trifluoromethyl-sulfonyloxy, ethanesulfonyloxy, benzenesulfonyloxy, toluenesulfonyloxy, and triazolyl;

in step (3b) the aminating agent is selected from the group:  $\text{NH}_3$ , ammonium hydroxide, and ammonium carbonate; and

in step (4) the suitable base is selected from the group consisting of: sodium hydroxide, lithium hydroxide, potassium carbonate, sodium carbonate, sodium methoxide, sodium ethoxide,  $\text{C}_3\text{-C}_6$  alkyl primary amine, ammonium hydroxide, and ammonium  $\text{C}_1\text{-C}_6$  alkoxide.

39. The process of Claim 38 for the preparation of a compound of Formula (IV), wherein:

in step (1), the suitable polar aprotic solvent comprises one solvent which is acetonitrile;

in step (2), the reducing agent is Zn-Cu couple;

in step (2), the acid catalyst, when present, is acetic acid;

in step (2), the suitable polar solvent comprises a combination of methanol and ethyl acetate;

in step (3a) the activating agent is triazole/phosphorus oxychloride;

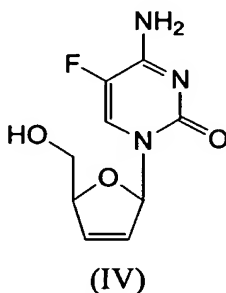
in step (3a) the amine base is triethylamine;

in step (3a) the leaving group LG is triazolyl;

in step (3b), the aminating agent is  $\text{NH}_3$ ; and

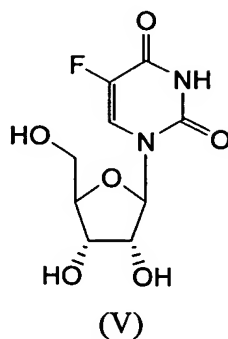
in step (4) the suitable base is sodium methoxide.

40. The process according to Claim 39, for the preparation of a compound of Formula (IV):

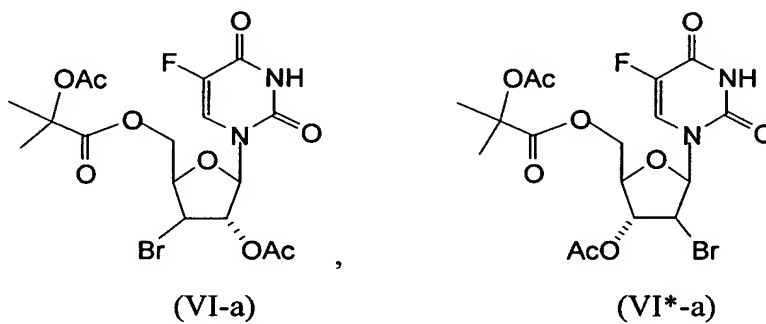


comprising:

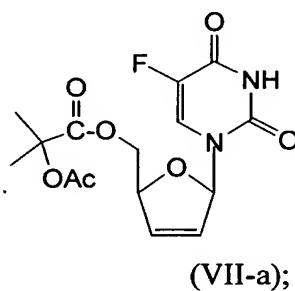
(1) contacting a compound of Formula (V):



with 2-acetoxy-2-methyl-propionyl bromide in acetonitrile to form a mixture of compounds of Formula (VI-a) and (VI\*-a):

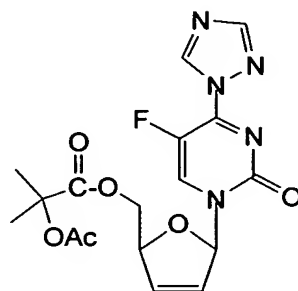


(2) contacting the mixture of compounds of Formula (VI-a) and (VI\*-a); with Zn-Cu couple in a suitable polar solvent comprising a combination of methanol and ethyl acetate, wherein the ratio of methanol to ethyl acetate is in the range of 1:2 to 1:4; optionally in the presence of acetic acid, to form a compound of Formula (VII-a):





(3a) contacting the compound of Formula (VII-a) with 1,2,4-triazole/phosphorus oxychloride, in the presence of triethylamine, to form a compound of Formula (VIII-a):

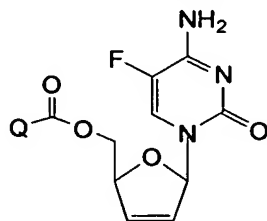


(VIII-a);

(3b) contacting the compound of Formula (VIII-a) with NH<sub>3</sub>, to form a compound of Formula (III-a), and

(4) contacting the compound of Formula (III-a) with sodium methoxide to form the compound of Formula (IV).

41. A process for the preparation of a compound of Formula (III):



(III)

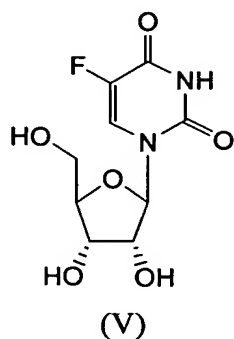
wherein:

Q is 2-(R<sup>1</sup>CH<sub>2</sub>CO<sub>2</sub>)phenyl-, R<sup>1</sup>CH<sub>2</sub>-, or R<sup>1</sup>CH<sub>2</sub>C(=O)OC(R<sup>2</sup>)<sub>2</sub>-;

R<sup>1</sup> is H or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sup>2</sup>, at each occurrence, is independently selected from methyl, ethyl, and propyl; comprising:

(1) contacting a compound of Formula (V):



with an acyl halide of Formula  $Q-C(=O)X$ , wherein:

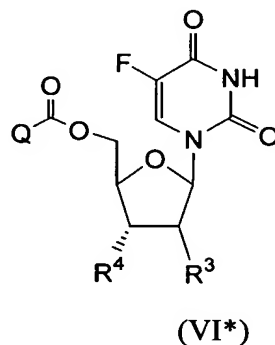
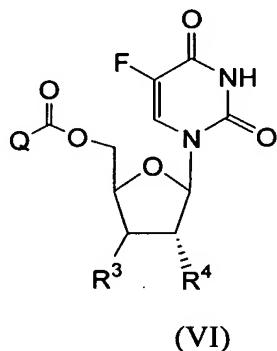
$Q$  is 2-( $R^1CH_2CO_2$ )phenyl-,  $R^1CH_2$ -, or  $R^1CH_2C(=O)OC(R^2)_2$ ;

$X$  is Cl, Br, or IV;

$R^1$  is H or  $C_1$ - $C_6$  alkyl;

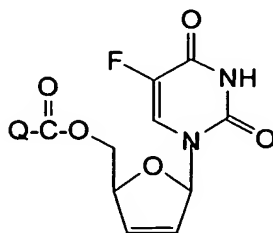
$R^2$ , at each occurrence, is independently selected from methyl, ethyl, and propyl;

in a suitable polar aprotic solvent to form a compound of Formula (VI), a compound of Formula (VI\*), or a mixture of compounds of Formula (VI) and (VI\*):



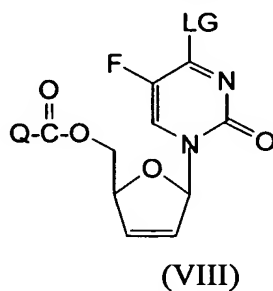
wherein  $R^3$  is X; and  $R^4$  is  $R^1CH_2C(=O)O$ -;

(2) contacting the compound of Formula (VI), the compound of Formula (VI\*), or the mixture of compounds of Formula (VI) and (VI\*); with a reducing agent in a suitable polar solvent, optionally in the presence of an acid catalyst, to form a compound of Formula (VII):



(VII);

(3a) contacting the compound of Formula (VII) with an activating agent in the presence of an amine base, to form a compound of Formula (VIII):



wherein LG is a leaving group derived from the activating agent;  
(3b) contacting the compound of Formula (VIII) with an aminating agent to form a compound of Formula (III).

42. The process of Claim 41 for the preparation of a compound of Formula (III), wherein:
- in step (1) the acyl halide of Formula  $Q-C(=O)X$  comprises:
    - 2-acetoxy-2-methyl-propionyl bromide,
    - 2-(acetoxy)-2-methyl-butanoyl bromide,
    - 2-(acetoxy)-2-ethyl-butanoyl bromide, or
    - 2-(acetoxy)-2-methyl-pentanoyl bromide;
  - in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent or a combination of two or more polar aprotic solvents; and is selected from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl methyl ether, dimethoxy ethane, 2-methoxyethyl ether, dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and isopropyl acetate;
  - in step (2), the reducing agent is selected from the group consisting of: Fe, Zn-Cu couple and Zn;
  - in step (2), the acid catalyst, when present, is selected from the group consisting of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic acid, HCl, HBr, HI, and  $H_2SO_4$ ;
  - in step (2), the suitable polar solvent comprises one polar solvent or a combination of two or more polar solvents; and is selected from the group

consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate, butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy ethane, and 2-methoxyethyl ether;

in step (3a) the activating agent is selected from the group consisting of:

methanesulfonyl chloride, trifluoromethyl sulfonyl chloride, ethanesulfonyl chloride, benzenesulfonyl chloride, p-toluene-sulfonyl chloride, triazole/phosphorus oxychloride and triazole/diphenyl chloro-phosphate;

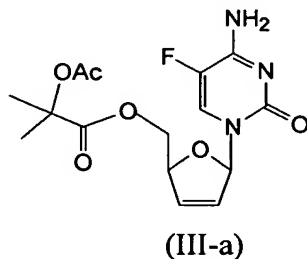
in step (3a) the amine base is selected from the group consisting of:

triethylamine, tributylamine, N-methylmorpholine, N,N-diisopropyl-ethylamine, N,N-dimethylcyclohexylamine, N,N-diethylcyclohexylamine, N,N-dimethyloctylamine, tetramethylethylenediamine, pyridine, N,N-dimethyl-aminopyridine, 1,4-diazabicyclo[2.2.2]octane, 1,8-diazabicyclo[5.4.0]undec-7-ene, and 1,5-diazabicyclo[4.3.0]non-5-ene;

in step (3a) the leaving group LG is selected from the group consisting of methanesulfonyloxy, trifluoromethyl-sulfonyloxy, ethanesulfonyloxy, benzenesulfonyloxy, toluenesulfonyloxy, and triazolyl;

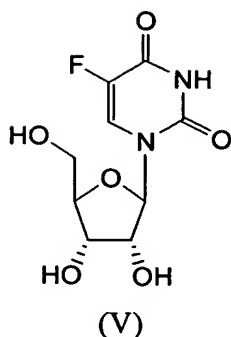
in step (3b) the aminating agent is selected from the group:  $\text{NH}_3$ , ammonium hydroxide, and ammonium carbonate.

43. The process according to Claim 41, for the preparation of a compound of Formula (III-a):

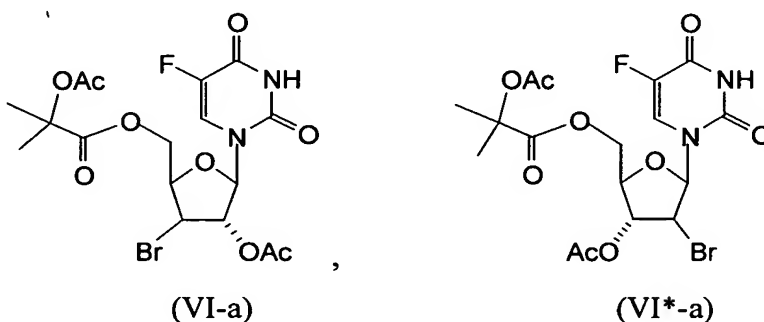


comprising:

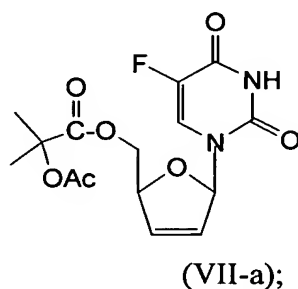
(1) contacting a compound of Formula (V):



with 2-acetoxy-2-methyl-propionyl bromide in a suitable polar aprotic solvent to form a compound of Formula (VI-a), a compound of Formula (VI\*-a), or a mixture of compounds of Formula (VI-a) and (VI\*-a):



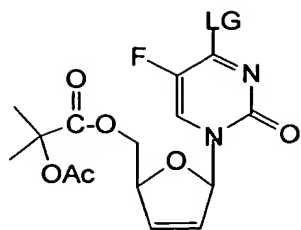
(2) contacting the compound of Formula (VI-a), the compound of Formula (VI\*-a), or the mixture of compounds of Formula (VI-a) and (VI\*-a); with a reducing agent in a suitable polar solvent, optionally in the presence of an acid catalyst, to form a compound of Formula (VII-a);



(3a) contacting the compound of Formula (VII-a) with a activating agent selected from the group consisting of:

- i) an aryl sulfonyl halide,
- ii) an alkyl sulfonyl halide, and
- iii) 1,2,4-triazole in the presence of a phosphorus chloride;

in the presence of an amine base, to form a compound of Formula (VIII-a):



(VIII-a)

wherein LG is a leaving group derived from the activating agent; and  
 (3b) contacting the compound of Formula (VIII-a) with an aminating agent to  
 form a compound of Formula (III-a).

44. The process of Claim 43 for the preparation of a compound of Formula (III-a),  
 wherein:
- in step (1), the suitable polar aprotic solvent comprises one polar aprotic solvent  
 or a combination of two or more polar aprotic solvents; and is selected  
 from the group consisting of: methylene chloride, tetrahydrofuran, t-butyl  
 methyl ether, dimethoxy ethane, 2-methoxyethyl ether,  
 dimethylformamide, dimethylacetamide, acetonitrile, ethyl acetate, and  
 isopropyl acetate;
  - in step (2), the reducing agent is selected from the group consisting of: Fe, Zn-Cu  
 couple and Zn;
  - in step (2), the acid catalyst, when present, is selected from the group consisting  
 of: acetic acid, propanoic acid, butyric acid, benzoic acid, toluene sulfonic  
 acid, HCl, HBr, HI, and H<sub>2</sub>SO<sub>4</sub>;
  - in step (2), the suitable polar solvent comprises one polar solvent or a  
 combination of two or more polar solvents; and is selected from the group  
 consisting of: methanol, ethanol, propanol, ethyl acetate, propyl acetate,  
 butyl acetate, isopropyl acetate, acetonitrile, tetrahydrofuran, dimethoxy  
 ethane, and 2-methoxyethyl ether; and
  - in step (3a) the activating agent is selected from the group consisting of:  
 methanesulfonyl chloride, trifluoromethyl sulfonyl chloride,  
 ethanesulfonyl chloride, benzenesulfonyl chloride,  
 p-toluene-sulfonyl chloride, triazole/phosphorus oxychloride and  
 triazole/diphenyl chloro-phosphate;

in step (3a) the amine base is selected from the group consisting of:

triethylamine, tributylamine,  
N-methylmorpholine, N,N-diisopropyl-ethylamine,  
tetramethylethylenediamine, pyridine,  
N,N-dimethyl-aminopyridine,  
1,4-diazabicyclo[2.2.2]octane, and  
1,8-diazabicyclo[5.4.0]undec-7-ene;

in step (3a) the leaving group LG is selected from the group consisting of  
methanesulfonyloxy, trifluoromethyl-sulfonyloxy, ethanesulfonyloxy,  
benzenesulfonyloxy, toluenesulfonyloxy, and triazolyl; and

in step (3b) the aminating agent is selected from the group:  $\text{NH}_3$ , ammonium  
hydroxide, and ammonium carbonate.

45. The process of Claim 44 for the preparation of a compound of Formula (III-a),  
wherein:

in step (1), the suitable polar aprotic solvent comprises one solvent which is  
acetonitrile;

in step (2), the reducing agent is Zn-Cu couple;

in step (2), the acid catalyst, when present, is acetic acid;

in step (2), the suitable polar solvent comprises a combination of methanol and  
ethyl acetate;

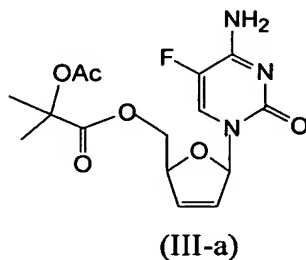
in step (3a) the activating agent is triazole/phosphorus oxychloride;

in step (3a) the amine base is triethylamine;

in step (3a) the leaving group LG is triazolyl; and

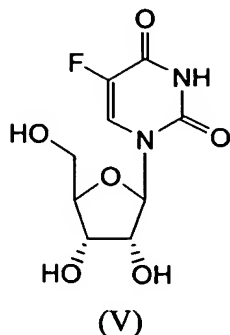
in step (3b), the aminating agent is  $\text{NH}_3$ .

46. The process according to Claim 45, for the preparation of a compound of  
Formula (III-a):

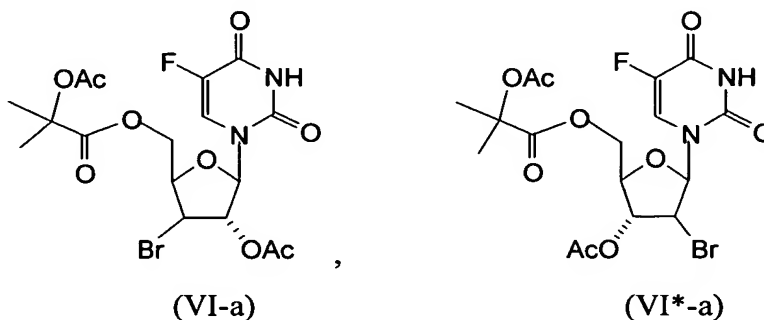


comprising:

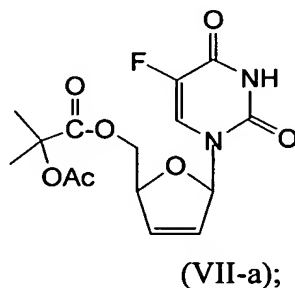
(1) contacting a compound of Formula (V):



with 2-acetoxy-2-methyl-propionyl bromide in acetonitrile to form a compound of Formula (VI-a), a compound of Formula (VI\*-a), or a mixture of compounds of Formula (VI-a) and (VI\*-a):

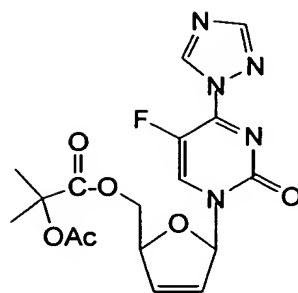


(2) contacting the compound of Formula (VI-a), the compound of Formula (VI\*-a), or the mixture of compounds of Formula (VI-a) and (VI\*-a); with Zn-Cu couple in a suitable polar solvent comprising a combination of methanol and ethyl acetate, wherein the ratio of methanol to ethyl acetate is in the range of 1:2 to 1:4; optionally in the presence of acetic acid, to form a compound of Formula (VII-a):



(3a) contacting the compound of Formula (VII-a) with 1,2,4-triazole/phosphorus oxychloride, in the presence of triethylamine, to form a compound of Formula (VIII-a):



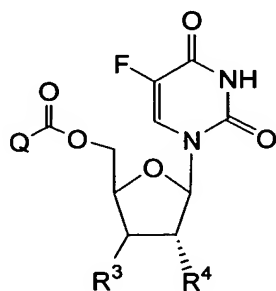


(VIII-a);

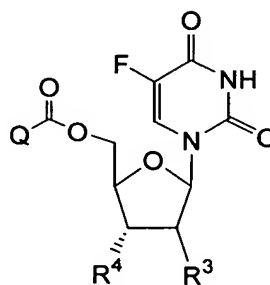
and

(3b) contacting the compound of Formula (VIII-a) with  $\text{NH}_3$ , to form a compound of Formula (III-a).

47. A compound of Formula (VI) or (VI\*):



(VI)



(VI\*)

or a pharmaceutically acceptable salt thereof, wherein:

Q is  $\text{R}^1\text{CH}_2-$  or  $\text{R}^1\text{CH}_2\text{C}(=\text{O})\text{OC}(\text{R}^2)_2-$ ;

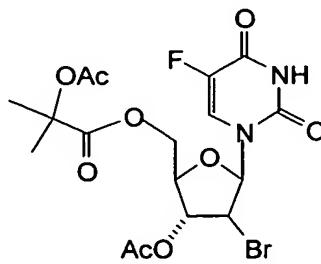
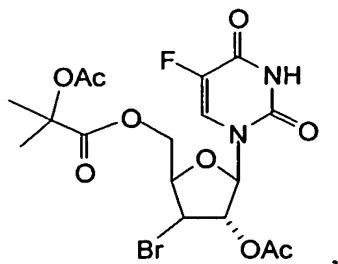
$\text{R}^1$  is H or  $\text{C}_1$ - $\text{C}_6$  alkyl;

$\text{R}^2$  is independently selected from methyl, ethyl, and propyl;

$\text{R}^3$  is Cl, Br, or IV; and

$\text{R}^4$  is  $\text{R}^1\text{CH}_2\text{C}(=\text{O})\text{O}-$ .

48. A compound of Claim 47 of Formula (VI-a) or (VI\*-a):

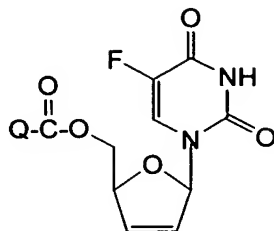


(VI-a)

(VI\*-a)

or a pharmaceutically acceptable salt thereof.

49. A compound of Formula (VII):



(VII)

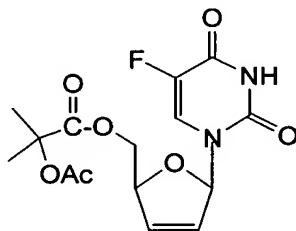
or a pharmaceutically acceptable salt thereof, wherein:

Q is  $R^1CH_2-$  or  $R^1CH_2C(=O)OC(R^2)_2-$ ;

$R^1$  is H or  $C_1-C_6$  alkyl; and

$R^2$  is independently selected from methyl, ethyl, and propyl.

50. A compound of Claim 49 of Formula (VII-a):

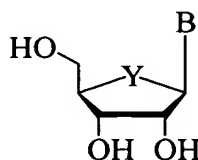


(VII-a)

or a pharmaceutically acceptable salt thereof.

51. A process for the preparation of a  $\beta$ -D- and  $\beta$ -L-2',3'-dideoxy-2',3'-dideohydro-nucleoside comprising:

- a) activating a compound of structure (1)



(1)

wherein B is a pyrimidine or purine base; and

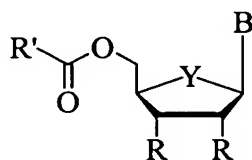
Y is O, S or  $CH_2$ ;

with an acyl halide of the formula  $X-C(=O)R^1$ ,  $X-C(=O)C(R^1)_2OC(=O)R^1$  or  $X-C(=O)phenylC(=O)OR^1$ ;

wherein X is a halogen (F, Cl, Br or I), and

each  $R^1$  is independently hydrogen, lower alkyl, alkyl, aryl or phenyl;

to form a compound of structure (2)

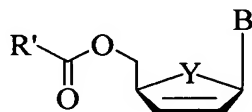


(2)

wherein  $R^1$  is  $R^1$ ,  $-C(R^1)_2OC(=O)R^1$  or  $-phenylC(=O)OR^1$ ; and

at least one R is halogen (F, Cl, Br or I), and at least one R is an acyl of the formula  $-OC(=O)R^1$ ; and then

- b) reducing the compound of structure (2) with a reducing agent to form a 2',3'-dideoxy-2',3'-dideoxy-nucleoside of structure (3)



(3)

- c) optionally deprotecting the nucleoside if necessary.

52. The process of Claim 51, wherein B is 5-fluorouracil or 5-fluorocytosine.

53. The process of Claim 51, wherein Y is O.

54. The process of Claim 51, wherein the  $\beta$ -D- and  $\beta$ -L-2',3'-dideoxy-2',3'-dideoxy-nucleoside is D4FC.

55. The process of Claim 51, wherein the  $\beta$ -D- and  $\beta$ -L-2',3'-dideoxy-2',3'-dideoxy-nucleoside is  $\beta$ -D-D4FC.

56. The process of Claim 51, wherein the  $\beta$ -D- and  $\beta$ -L-2',3'-dideoxy-2',3'-dideoxy-nucleoside is  $\beta$ -D-D4FC.

57. The process of Claim 51, further comprising reducing the  $\beta$ -D or  $\beta$ -L-2',3'-dideoxy-2',3'-didehydro-nucleoside into a  $\beta$ -D or  $\beta$ -L-2'- or 3'-deoxyribo-nucleoside.
58. The process of Claim 51, further comprising converting the  $\beta$ -D or  $\beta$ -L-2',3'-dideoxy-2',3'-didehydro-nucleoside bearing a different nucleobase.
59. The process of Claim 58, wherein the  $\beta$ -D or  $\beta$ -L-2',3'-dideoxy-2',3'-didehydro-nucleoside is  $\beta$ -D or  $\beta$ -L-2',3'-dideoxy-2',3'-didehydro-5-fluorouridine which is converted to a  $\beta$ -D or  $\beta$ -L-2',3'-dideoxy-2',3'-didehydro-5-fluorocytidine.